REMARKS

The Amendment

Claim 1 is reworded to clarify the meaning of the claim. Claim 1 is also amended to include the limitation of Claim 21.

Claim 19 is amended to recite essential steps of the method claimed. Support for the amendment can be found, for example, at page 2, second paragraph, and page 4, third paragraph.

No new matter is added in any of the amendments. The Examiner is respectfully requested to enter all the amendments.

35 U.S.C. §112 Second Paragraph Rejection

Claims 1-21 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Claim 21 is canceled. The rejections to Claims 1-20 are traversed in part, and overcome in part in view of the claim amendments.

The Examiner states that Claim 1 is confusing for several reasons. Applicants have reorganized Claim 1 to clarify the meaning of the claim. Applicants have also amended Claim 1 to recite that the parvovirus minimal origin of replication is CTWWTCA. Therefore, Claim 1 is clear as amended.

The Examiner states that it is unclear in Claim 2 what is meant by "internal replication sequences." Applicants do not agree with the Examiner because the phrase is defined in the reference of Tam and Astell, which is cited in the specification in the paragraph bridging pages 3 and 4.

The Examiner states that Claim 3 is unclear as to "an NS1 nicking site." Applicants have amended Claim 3 to recite that wherein the CTWWTCA sequence is a consensus sequence of an NS1 nicking site.

The Examiner states that Claim 21 is indefinite, because it recites a nucleotide sequence without a SEQ ID NO. Claim 21 is canceled; the sequence is incorporated into Claim 1. 37 C.F.R. §1.821(a) states that nucleotide sequences as used in 1.821(a) and 1.825 are interpreted to mean an unbranched sequence as 10 or more nucleotides. The sequence at issue here,

CTWWTCA, only has 7 nucleotides. Therefore, it is not required that the sequence be included in the sequence listing.

Claims 19-20 are rejected because the clkams do not set forth any steps involved in the method. Applicants have amended Claims 19 and 20 to recite essential steps of the method.

Therefore, the §112, second paragraph rejections of Claims 1-20 should be withdrawn.

35 U.S.C. §112 First Paragraph Rejection

Claims 1-21 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or to which it is most narrowly permitted, to make and/or use the invention. Claim 21 is canceled. The rejections to Claims 1-20 are traversed in part, and overcome in part in view of the claim amendments.

The Examiner states that Claim 1 requires a left terminus with a minimal origin of replication; it appears from the specification that some manipulation of the terminal sequence is intended. Applicants submit that some manipulation of a terminal sequence is optional, but not required. In the specification at page 3, middle of the second paragraph, it states "for the provision of the minimal parvovirus origin of replication at the left terminus of the parvovirus DNA it is favorable to extend the left terminus by an inverted repeat of the unique sequence located immediately downstream from the 3' terminal palindrome of the parvovirus DNA." Pursuant to the description, this manipulation is not absolutely necessary.

Claims 19 and 20 are rejected because the Examiner states that successful gene therapy using a parvoviral vector was not a matter of routine for practitioners of the art at the time the invention was made. Applicants submit that a person skilled in the art would have taken the same steps as those taken in connection with different vectors suitable for gene therapy to practice the claimed invention

Therefore, the §112, first paragraph rejection of Claims 1-20 should be withdrawn.

35 U.S.C. §101 Rejection

Claims 19-20 are rejected under 35 U.S.C. §101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. §101.

Applicants have amended Claims 19 and 20 to add an essential step of the claims. Therefore, the §101 rejection of Claims 19 and 20 should be withdrawn.

35 U.S.C. §102(b) Rejections

Claims 1-4 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Samulski, *et al.* (Journal of Virology, 61:3096-3101).

Claims 1-4, 9, 14, 15, 17 and 18 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Shenk, *et al.,* U.S. Patent No. 5,436,146.

Claims 1-4 and 7 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Srivastava, *et al.,* (PNAS 86:8076-8082, 1989).

Claims 1-6, 9, 14, 15, 18 and 21 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Maxell, *et al.* (U.S. Patent No. 5,585,254).

Claims 1-6 and 21 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Tam, *et al.* (Virology 193,.812-824, 1993).

Claim 21 is canceled. All the above §102 (b) rejections to the remaining claims are overcome in view of the claim amendment of adding limitation of CTWWTCA in Claim 1. None of the cited references have disclosed the CTWWTCA sequence. Therefore, the §102(b) rejections should be withdrawn.

35 U.S.C. §103(a) Rejection

Claims 9-12, 15, 18, and 19 are rejected under 35 U.S.C. §103(a) as being unpatentable over Dwarki, *et al.,* (U.S. Patent No. 6,221,646).

Claim 13 is rejected under 35 U.S.C. §103(a) as being unpatentable over Dwarki, *et al.,* (U.S. Patent No. 6,221,646) as applied to Claims 9-12, 15, 18 and 19, and further in view of Williams, *et al.*

Claims 10, 11, 19 and 20 are rejected under under 35 U.S.C. §103(a) as being unpatentable over Shenk, *et al.,* (U.S. Patent No. 5,436,146) as applied to Claims 1-4, 9, 14, 15, 17, and 18, and further in view of Kurtzman, *et al.*, (U.S. Patent No. 5,952,221).

Claim 16 is rejected under 35 U.S.C. §103(a) as being unpatentable over Shenk, *et al.*, (U.S. Patent No. 5,436,146) as applied to Claims 1-4, 9, 14, 15, 17, and 18, and further in view of Chiorini, *et al.*, (U.S. Patent No. 5,693,531).

None of the above cited references have taught or suggested the claimed element of CTWWTCA sequence; therefore, the combination of the references does not produce the claimed invention.

The unexpected results and advantages of the present invention are described in the specification at page 7, last paragraph:

> Parvovirus vectors according to the invention distinguish themselves in that they permit higher levels of amplification of the parvovirus genomes that are excised from the parvovirus vectors. Moreover, the above-mentioned packaging cell lines (e.g monkey COS, 293T) are highly susceptible to transfection by the convenient and cost-sparing Calciumphsophate coprecipitation techniques or DEAE-DEXTRAN and allow the use of shuttle helper plasmids of the type discussed above. The combination of the described changes in parvovirus vector and packaging systems greatly improves the yields of parvovirus vector (parvovirus DNA insert) production giving up to 1000 times higher titers of infectious parvoviral particles as compared with the conventional parvovirus vectors packaging system, in particularly those described in Russell, S.J., *et al.*, above. This represents a great advantage, particularly as regards time and costs.

Because the cited references do not teach or suggest the claimed element CTWWTCA sequence, and because the present invention has unexpected results and advantages over any prior art, the §103(a) rejections should be withdrawn.

Conclusion

Applicants believe that the application is in good and proper condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 463-8109.

Respectfully submitted,

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